

What we claim is:

1. A method of treating, inhibiting or preventing pathogenic change resulting from vascular injury in a human subject, the method comprising  
5 administering an aldosterone antagonist a human subject susceptible to or suffering from said pathogenic change, wherein said aldosterone antagonist is administered in an amount that is therapeutically effective in suppressing said pathogenic change.
2. The method of Claim 1 wherein said vascular injury results substantially  
10 from trauma.
3. The method of Claim 1 wherein said vascular injury results substantially from surgery.
4. The method of Claim 1 wherein said vascular injury results substantially  
15 from angioplasty.
5. The method of Claim 1 wherein the vascular injury is injury to a blood vessel.  
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6. The method of Claim 5 wherein the vessel is an artery.
7. The method of Claim 5 wherein the vessel is a coronary artery.
8. The method of Claim 5 wherein the vessel is a pulmonary artery.  
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9. The method of Claim 1 wherein the vascular injury is injury to an artery and the gap angle of injury at the site of maximal injury to the artery is at least about 10 degrees.  
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10. The method of Claim 1 wherein the vascular injury is injury to a coronary artery resulting substantially from angioplasty.

11. The method of Claim 1 wherein the pathogenic change is selected from the group consisting of luminal narrowing, restrictive neointima formation, vascular collagen accumulation, extracellular matrix production, migration and proliferation of smooth muscle cells, and pathogenic changes resulting in a  
5 reduction in the area encompassed by the external elastic lamina of an artery.

12. The method of Claim 1 wherein the vascular injury is injury to an artery and the pathogenic change is luminal narrowing.

10 13. The method of Claim 1 wherein the vascular injury is injury to an artery and the pathogenic change is restrictive neointima formation.

14. The method of Claim 1 wherein the vascular injury is injury to an artery and the pathogenic change is vascular collagen accumulation.

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15. The method of Claim 1 wherein the vascular injury is injury to an artery and the pathogenic change is extracellular matrix production.

16. The method of Claim 1 wherein the vascular injury is injury to an artery  
20 and the pathogenic change is migration and proliferation of smooth muscle cells.

17. The method of Claim 1 wherein the vascular injury is injury to an artery and the pathogenic change results in a reduction in the area encompassed by the external elastic lamina of an artery.

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18. The method of Claim 1 wherein the vascular injury is injury to an artery and the aldosterone antagonist is administered in an amount that is therapeutically effective to maintain, for at least about one month after the injury occurs, the ratio of intima area to vessel area for the artery at the site of maximal injury to the artery  
30 below about 0.37.

19. The method of Claim 1 wherein the vascular injury is injury to a coronary artery and the aldosterone antagonist is administered in an amount that is therapeutically effective to maintain, for at least about one month after the injury occurs, the ratio of intima area to vessel area for the coronary artery at the site of maximal injury to the artery below about 0.30.

20. The method of Claim 19 wherein the vascular injury is injury to a coronary artery resulting substantially from angioplasty.

21. The method of Claim 1 wherein the vascular injury is injury to an artery and the aldosterone antagonist is administered in an amount that is therapeutically effective to maintain, for at least about six months after the injury occurs, the ratio of intima area to vessel area for the artery at the site of maximal injury to the artery below about 0.37.

22. The method of Claim 1 wherein the vascular injury is injury to a coronary artery and the aldosterone antagonist is administered in an amount that is therapeutically effective to maintain, for at least about six months after the injury occurs, the ratio of intima area to vessel area for the coronary artery at the site of maximal injury to the artery below about 0.30.

23. The method of Claim 22 wherein the vascular injury is injury to a coronary artery resulting substantially from angioplasty.

24. The method of Claim 1 wherein the vascular injury is injury to an artery resulting substantially from angioplasty and the aldosterone antagonist is administered to the subject before the angioplasty.

25. The method of Claim 1 wherein the vascular injury is injury to an artery resulting substantially from angioplasty and the aldosterone antagonist is administered to the subject before and after the angioplasty.

26. A method of treating, inhibiting or preventing pathogenic change resulting from vascular injury in a subject, the method comprising administering an aldosterone antagonist to a mammalian subject susceptible to or suffering from said pathogenic change, wherein said aldosterone antagonist is administered in an amount that is therapeutically effective in suppressing said pathogenic change, and wherein the amount of aldosterone antagonist administered daily to the subject does not exceed about 15 mg/kg body weight of the subject.

27. A method of treating, inhibiting or preventing restenosis of an artery resulting from vascular injury in a subject, the method comprising administering an aldosterone antagonist to a mammalian subject susceptible to or suffering from said restenosis, wherein said aldosterone antagonist is administered in an amount that is therapeutically effective in suppressing said restenosis, and wherein the amount of aldosterone antagonist administered daily to the subject does not exceed about 15 mg/kg body weight of the subject.

28. A method of treating, inhibiting or preventing restenosis of an artery resulting from vascular injury in a human subject, the method comprising administering an aldosterone antagonist to a human subject susceptible to or suffering from said restenosis, wherein said aldosterone antagonist is administered in an amount that is therapeutically effective in suppressing said restenosis.

29. The method of Claim 27 comprising administering the aldosterone antagonist to a human subject susceptible to or suffering from restenosis, wherein the aldosterone antagonist is administered in an amount that is therapeutically effective in suppressing said restenosis, and wherein the vascular injury substantially results from surgery or trauma.

30. The method of Claim 27 comprising administering the aldosterone antagonist to a human subject who has undergone angioplasty of an artery, wherein the aldosterone antagonist is administered in an amount that is therapeutically

effective in suppressing restenosis, and the vascular injury substantially results from said angioplasty.

31. The method of Claim 30 wherein the aldosterone antagonist is  
5 administered in an amount that is therapeutically effective to maintain, for at least about one month after the injury occurs, the ratio of intima area to vessel area for the angioplastied artery at the site of maximal injury to the artery below about 0.37.

32. The method of Claim 30 wherein the aldosterone antagonist is  
10 administered in an amount that is therapeutically effective to maintain, for at least about one month after the injury occurs, the ratio of intima area to vessel area for the angioplastied artery at the site of maximal injury to the artery below about 0.37.

33. The method of Claim 32 wherein the aldosterone antagonist is  
15 administered in an amount that is therapeutically effective to maintain, for at least about one month after the injury occurs, the ratio of intima area to vessel area for the angioplastied coronary artery at the site of maximal injury to the artery below about 0.30.

20 34. The method of Claim 30 wherein the aldosterone antagonist is administered in an amount that is therapeutically effective to maintain, for at least about six months after the injury occurs, the ratio of intima area to vessel area for the artery at the site of maximal injury to the artery below about 0.37.

25 35. The method of Claim 31 wherein angioplastied artery is a coronary artery.

36. The method of Claim 35 wherein the aldosterone antagonist is  
30 administered in an amount that is therapeutically effective to maintain, for at least about one month after the injury occurs, the ratio of intima area to vessel area for the angioplastied coronary artery at the site of maximal injury to the artery below about 0.30.

37. The method of Claim 27 wherein the aldosterone antagonist is administered to the subject before and after the angioplasty.

38. A method of treating, inhibiting or preventing vascular constrictive remodeling resulting from vascular injury in a subject, the method comprising  
5 administering an aldosterone antagonist to a mammalian subject susceptible to or suffering from said vascular constrictive remodeling, wherein said aldosterone antagonist is administered in an amount that is therapeutically effective in suppressing said vascular constrictive remodeling, and wherein the amount of  
10 aldosterone antagonist administered daily to the subject does not exceed about 15 mg/kg body weight of the subject.

39. A method of treating, inhibiting or preventing vascular constrictive remodeling resulting from vascular injury in a human subject, the method  
15 comprising administering an aldosterone antagonist to a human subject susceptible to or suffering from said vascular constrictive remodeling, wherein said aldosterone antagonist is administered in an amount that is therapeutically effective in suppressing said vascular constrictive remodeling.

20 40. A method of treating, inhibiting or preventing vascular collagen accumulation resulting from vascular injury in a human subject, the method comprising administering an aldosterone antagonist to a human subject susceptible to or suffering from said vascular collagen accumulation, wherein said aldosterone antagonist is administered in an amount that is therapeutically effective in  
25 suppressing said vascular collagen accumulation.

41. The method of Claim 40 wherein the vascular injury is injury to an artery and said aldosterone antagonist is administered in an amount that is therapeutically effective in suppressing said vascular collagen accumulation in the  
30 artery.

42. The method of Claim 41 wherein the vascular injury is injury to an artery and said aldosterone antagonist is administered in an amount that is therapeutically effective in suppressing said vascular collagen accumulation in the media and intima of the artery.

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43. The method of Claim 41 wherein the vascular injury is injury to an artery and said aldosterone antagonist is administered in an amount that is therapeutically effective in suppressing said vascular collagen accumulation in the media of the artery.

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44. The method of Claim 41 wherein the vascular injury is injury to an artery and said aldosterone antagonist is administered in an amount that is therapeutically effective in suppressing said vascular collagen accumulation in the intima of the artery.

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45. A method of treating, inhibiting or preventing vascular collagen accumulation resulting from vascular injury in a subject, the method comprising administering an aldosterone antagonist to a mammalian subject susceptible to or suffering from said vascular collagen accumulation, wherein said aldosterone antagonist is administered in an amount that is therapeutically effective in suppressing said vascular collagen accumulation, and wherein the amount of aldosterone antagonist administered daily to the subject does not exceed about 15 mg/kg body weight of the subject.

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25 46. The method of Claim 1 wherein the aldosterone antagonist is an aldosterone receptor antagonist.

47. The method of Claim 1 wherein the aldosterone antagonist is an epoxy-steroidal aldosterone antagonist.

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48. The method of Claim 1 wherein the epoxy-containing compound has an epoxy moiety fused to the "C" ring of the steroidal nucleus of a 20-spiroxane compound.

5           49. The method of Claim 1 wherein the 20-spiroxane compound is characterized by the presence of a 9- $\alpha$ ,11- $\beta$ -substituted epoxy moiety.

50. The method of Claim 1 wherein the epoxy-containing compound is selected from the group consisting of:

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Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,  $\gamma$ -lactone, methyl ester, (7 $\alpha$ ,11 $\alpha$ ,17 $\beta$ )-;

15           Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-dimethyl ester, (7 $\alpha$ ,11 $\alpha$ ,17 $\beta$ )-;

3'H-cyclopropa[6,7]pregna-4,6-diene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-,  $\gamma$ -lactone, (6 $\beta$ ,7 $\beta$ ,11 $\alpha$ ,17 $\beta$ )-;

20           Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo, 7-(1-methylethyl) ester, monopotassium salt, (7 $\alpha$ ,11 $\alpha$ ,17 $\beta$ )-;

Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, 7-methyl ester, monopotassium salt, (7 $\alpha$ ,11 $\alpha$ ,17 $\beta$ )-;

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3'H-cyclopropa[6,7]pregna-1,4,6-triene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-,  $\gamma$ -lactone, (6 $\beta$ ,7 $\beta$ ,11 $\alpha$ )-;

30           3'H-cyclopropa[6,7]pregna-4,6-diene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, methyl ester, (6 $\beta$ ,7 $\beta$ ,11 $\alpha$ ,17 $\beta$ )-;

3'H-cyclopropa[6,7]pregna-4,6-diene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, monopotassium salt, (6 $\beta$ ,7 $\beta$ ,11 $\alpha$ ,17 $\beta$ )-;

3'H-cyclopropa[6,7]pregna-4,6-diene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-  
5 17-hydroxy-3-oxo-,  $\gamma$ -lactone, (6 $\beta$ ,7 $\beta$ ,11 $\alpha$ ,17 $\beta$ )-;

Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,  $\gamma$ -lactone, ethyl ester, (7 $\alpha$ ,11 $\alpha$ ,17 $\beta$ )-; and

10 Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,  $\gamma$ -lactone, 1-methylethyl ester, (7 $\alpha$ , 11 $\alpha$ , 17 $\beta$ )-.

51. The method of Claim 1 wherein the aldosterone antagonist is eplerenone.

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52. The method of Claim 1 wherein the aldosterone antagonist is eplerenone in a daily dose range from about 0.5 mg to about 500 mg.

53. The method of Claim 27 wherein the aldosterone antagonist is  
20 eplerenone.

54. The method of Claim 38 wherein the aldosterone antagonist is eplerenone.

25 55. The method of Claim 40 wherein the aldosterone antagonist is eplerenone.

56. The method of Claim 1 wherein the aldosterone antagonist is spironolactone.

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57. The method of Claim 27 wherein the aldosterone antagonist is spironolactone.

58. The method of Claim 38 wherein the aldosterone antagonist is spironolactone.

5        59. The method of Claim 40 wherein the aldosterone antagonist is spironolactone.

60. The method of Claim 1 wherein the aldosterone antagonist is an aldosterone antagonist other than spironolactone.

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61. The method of Claim 27 wherein the aldosterone antagonist is an aldosterone antagonist other than spironolactone.

62. The method of Claim 38 wherein the aldosterone antagonist is an aldosterone antagonist other than spironolactone.

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63. The method of Claim 40 wherein the aldosterone antagonist is an aldosterone antagonist other than spironolactone.

20        64. The method of Claim 27 further comprising placing an endolumenal stent in the artery at the site of the injury to the artery.

65. The method of Claim 27 wherein the stent comprises an aldosterone antagonist.

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66. The method of Claim 27 wherein the stent comprises eplerenone.

67. The method of Claim 27 further comprising exposing the artery at the site of the injury to a source of radiation.

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68. The method of Claim 1 further comprising administering to the subject a compound selected from the group consisting of renin inhibitors, angiotensin I

antagonists, angiotensin II antagonists, angiotensin converting enzyme inhibitors, non-steroidal diuretics, and retinoic acid.

69. The method of Claim 1 further comprising administering an angiotensin  
5 II antagonist to the subject.

70. The method of Claim 1 further comprising administering an angiotensin converting enzyme inhibitor to the subject.

10 71. The method of Claim 1 further comprising administering an angiotensin converting enzyme inhibitor and a diuretic to the subject, wherein said diuretic is substantially without aldosterone antagonist effect.

72. The method of Claim 1 wherein the aldosterone antagonist is  
15 administered at a dose that results in a decrease in blood procollagen type III aminoterminal propeptide level in the subject relative to baseline level.

73. The method of Claim 1 wherein the aldosterone antagonist is administered at a dose that results in a decrease in blood N-terminal atrial  
20 natriuretic factor level in the subject relative to baseline levels.

74. The method of Claim 1 wherein the aldosterone antagonist is administered at a dose that results in a decrease in blood brain natriuretic peptide levels in the subject relative to baseline levels.

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